Amendments to the Specification:

On Page 41, please replace the paragraph beginning on line 16 and ending on line 20 with the following amended paragraph:

2. Control expression plasmids harboring the *bak* cDNA in the anti-sense orientation, or various unrelated cDNAs, do not eliminate ß-gal positive cells. In addition, certain Bak mutants (i.e., [^1D]ΔGD) have greatly diminished capacity to eliminate blue cells in this assay;

On Page 46, please replace the paragraph beginning on line 6 and ending on line 17 with the following amended paragraph:

Deletion of the carboxyl-terminal hydrophobic stretch of amino acids (residues 191-211) partially diminished, but did not eliminate, the cell killing function of Bak (mutant [^1D]ΔC). This hydrophobic "tail" likely serves as a membrane anchor sequence in Bak. Indeed, immunofluorescense studies of [^1D]ΔC in transiently transfected COS cells showed that the intracellular distribution of the [^1]ΔDC mutant is altered (diffuse cytoplasmic) relative to the wild type Bak, which appears largely mitochondrial. The carboxyl terminal hydrophobic tail is not required for the cell killing function of Bak, but may contribute indirectly, by ensuring proper sub-cellular localization of the protein.

On Page 46, please replace the paragraph beginning on line 18 and ending on line 4 of Page 47 with the following amended paragraph:

A segment of the Bak protein encompassed by the ^1DGD deletion (residues 82-94) is absolutely required for cell death function since this mutant is devoid of cell killing activity in the transient transfection assay. Specifically, co-transfection of ß-gal with Bak [^1D]ΔGD yielded as

many, or more, blue cells relative to co-transfection of ß-gal with the control vector plasmid. Deletion of adjoining residues (amino acids 67-81) immediately N-terminal to this domain reduced, but did not eliminate, cell death activity (Bak mutant [^1D]ΔPS). All other deletion mutants tested (with the exception of ^1DC, discussed above) were unaltered in their capacity to kill cells. Taken together, these results indicated that a co-linear segment (termed the "GD domain") defined by deletion mutants [^1D]ΔGD and [^1D]ΔPS (residues 67-94) is uniquely required for Bak cell killing function detected in the transient assay.

On Page 47, please replace the paragraph beginning on line 5 and ending on line 27 with the following amended paragraph:

To determine if the GD domain is sufficient for cell killing function, two truncated Bak protein derivatives, PEM and QVG, corresponding to amino acids 58-103 and 73-123, respectively, were tested for activity in the transient transfection assay. QVG significantly reduced the number of blue cells when co-transfected with ß-gal, indicating that it retained some capacity to kill Rat-1 cells. While the reduction in blue cell number was diminished relative to full length Bak, both PEM and QVG lack the carboxyl-terminal membrane anchor and, by analogy to the Bak [^1]ΔDC mutant, would likely not exhibit full cell killing function due to altered sub-cellular localization. Indeed, QVG was similar to the Bak [^1D]ΔC mutant with respect to its activity. In an effort to improve the cell killing capacity of the truncated Bak species, the hydrophobic tail element (amino acids 187-211) was fused to the C-termini of both PEM and QVG (PEM+C and QVG+C, respectively). In each case, attachment of the putative membrane anchor improved the ability of the truncated Bak mutants to eliminate blue cells in the transfection assay, and resulted in activity comparable to wild-type Bak

(Figure 2). Thus, these results indicated that a protein domain shared by both PEM and QVG (residues 73-103) is sufficient for the cell killing function of Bak.

On Page 48, please replace the paragraph beginning on line 22 and ending on line 7 of Page 49 with the following amended paragraph:

The Bak deletion mutants described above were tested for their Bcl-x_L binding capacity, both *in vitro* and in transfected COS cells, and the results are summarized in Figure 4. Deletion of residues 82-94 ([^1D]ΔGD mutant) completely eliminated the ability of Bak to interact with Bcl-x_L. Interaction with Bcl-x_L was also diminished by deletion of adjoining amino acids 67-81 ([^1D]ΔPS Bak mutant). All other deletion mutants tested, encompassing the entire Bak open reading frame, retained the ability to bind Bcl-x_L in these assays. These results identify Bak sequences encompassed by the [^1D]ΔGD and [^1D]ΔPS mutants (maximally, amino acids 67-94) as uniquely important in mediating the interaction with Bcl-x_L. The same Bak region, the GD domain, was required for the cell killing function of Bak.

On Page 51, please replace the paragraph beginning on line 1 and ending on line 14 with the following amended paragraph:

GD domain elements within Bax and Bipla were evaluated to determine whether they are also critical to the cell killing and protein binding functions of these proteins. Small deletions that removed the conserved GD domain motifs were introduced into Bax and Bipla, and the mutants were then analyzed for their ability to kill Rat-1 cells and bind to Bcl-x_L. This analysis revealed that, like Bak [^1D]ΔGD, the Bax [^1D]ΔGD and Bipla [^1D]ΔGD mutants are impaired in their ability to eliminate blue cells when co-transfected with ß-gal in Rat-1 cells (Figure 6). In addition, both

mutants no longer have the capacity to interact with Bcl-x_L (Figure 6). Thus, function of the GD domain element is conserved in Bak, Bax and Bipla, and is critical to the biological activities of all three proteins.